PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 207399WO	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/EP 03/12412	International filing date *(day/month/year)* 03.11.2003	Priority date *(day/month/year)* 21.11.2002
International Patent Classification (IPC) or both national classification and IPC C07C253/30		
Applicant DSM IP ASSETS B.V. et al		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 1 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
09.06.2004	14.12.2004
Name and mailing address of the international preliminary examining authority: European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized Officer Fitz, W Telephone No. +31 70 340-4359

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP 03/12412

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-22 as originally filed

Claims, Numbers

1-10 received on 28.10.2004 with letter of 27.10.2004

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-10
	No:	Claims	-
Inventive step (IS)	Yes:	Claims	1-10
	No:	Claims	-
Industrial applicability (IA)	Yes:	Claims	1-10
	No:	Claims	-

2. Citations and explanations

see separate sheet

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

D1: US-A-4 683 324

D2: DATABASE WPI Derwent Publications Ltd., London, GB; AN 1993-383032 XP002237430 "IMPROVED RACEMISATION FOR 2-AMINO:NITRILE(S) - COMPRISES CONTACTING OPTICALLY ACTIVE 2-AMINO:NITRILE(S) WITH POTASSIUM CYANIDE IN BENZENE-METHANOL MIXTURE" -& JP 05 286919 A ((NIHA) NIKKO KYOSEKI KK) 2 November 1993 (1993-11-02)

D3: LOPEZ-SERRANO P ET AL: TETRAHEDRON: ASYMMETRY, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 12, no. 2, 19 February 2001 (2001-02-19), pages 219-228, XP004230902 ISSN: 0957-4166

1.) Documents D1 and D2 disclose processes for the racemisation of α-amino nitriles from which the process of present claim 1 mainly differs in that the solvent is aprotic (whereas in D1 and D2 protic solvents are used).

Document D3 discloses a process for the racemisation of α-amino nitriles from which the process of present claim 1 differs in that the catalyst is a Lewis acid catalyst (whereas in D3 Zeolite NaA, having basic sites, is used as the catalyst).

The subject-matter of claim 1 is therefore new (Article 33(2) PCT).

2.) Document D1 is considered to represent the closest prior art, because it also discloses a process for the acid-catalysed racemisation of α-amino nitriles.

In view of the teachings of D1, the problem underlying the present application may be regarded as the provision of a further process for the racemisation of α-amino nitriles.

The solution to this problem proposed in present claim 1 is considered as involving an inventive step (Article 33(3) PCT) because D1 alone, or in combination with another document of the prior art, would not suggest to the skilled person that the desired racemisation would be effected in an aprotic solvent in the presence of a Lewis acid catalyst.

Claims 2-10 are dependent on claim 1 and as such also meet the requirements of the

PCT with respect to novelty and inventive step.

3.) Claims 1-10 are industrially applicable because the racemisation of α-amino nitriles is useful for the preparation of pharmaceuticals and agrochemicals.

CLAIMS

1. Process for the racemisation of an enantiomerically enriched α-amino nitrile characterized in that the enantiomerically enriched α-amino nitrile is contacted with a Lewis acid catalyst.
2. Process according to claim 1, wherein an aprotic solvent is used.
3. Process according to claim 1 or 2, wherein the Lewis acid catalyst comprises a metal chosen from main group elements IA-IVA of the Periodic Table (CAS version), the transition metals and the lanthanides.
4. Process according to claim 3 wherein the metal is chosen from the group consisting of Al, Ti, Zr, or lanthanides.
5. Process according to any one of claims 1-4, wherein a catalyst with the general structure $M_nX_pS_qL_r$ is used, wherein M represents the metal, X represents an anionic counterion or covalently bound anionic ligand for non zero valent metals, S represents a spectator ligand, L represents a neutral ligand, n represents an integer larger than or equal to 1 and p, q and r each independently represent an integer larger than or equal to 0, and in which n and p are chosen such that M_nX_p is neutral.
6. Process according to claim 5 wherein the catalyst is chosen from the group of aluminum alkoxides, aluminum alkyls, lanthanide alkoxydes and lanthanocenes.
7. Process according to any one of claims 1-6, wherein the racemisation is performed in combination with a resolution process.
8. Process according to claim 7, wherein the racemisation is performed in combination with an enzymatic resolution process.
9. Process according to claim 7, wherein the racemisation is performed in combination with a crystallization induced resolution.
10. Process according to any one of claims 7-9, wherein the resolution process is combined with racemisation in situ.
11. Process according to claim 10, wherein the racemisation is performed in situ in a crystallization induced asymmetric transformation process.

Replaced by Art 34